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EXAMINER

18M1/1127

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ART UNIT	PAPER NUMBER
1806	

DATE MAILED: 11/27/96

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☒ Responsive to communication filed on _____ ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), 0 days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☒ Notice of References Cited by Examiner, PTO-892.
2. ☒ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☒ Claims 9-27 are pending in the application.
   Of the above, claims _____ are withdrawn from consideration.
2. ☒ Claims 1-18 have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 19-27 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
12. ☒ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☒ been received ☐ not been received ☐ been filed in parent application, serial no. _____ ; filed on _____.
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

1. Claims 1-18 have been canceled.

Claims 19-27 have been added.

Claims 19-27 are pending.

2. The drawings remain objected to because the subfigures of Figures 1-4 must be separately labeled. Correction is required.

3. The disclosure remains objected to because of the following informalities:

The subfigures of Figure 4 are labeled 4(1)-4(4), while subfigures for Figures 1-3 are labeled with Arabic letters. Subfigures 1A-1F, 2A-2B, 3A-3B and those in Figure 4 are not separately described in The Brief Description of Drawings.

NEW REJECTIONS

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5. Claims 19-27 are rejected under 35 U.S.C. § 112, first paragraph, as the specification lacks complete deposit information for the deposit of the hybridoma cell line CNCM

Accession No. I-1397 for the reasons set forth in the objection to the specification. The Response and Amendment filed August 28, 1996 states that a Declaration of Dr. Fischman and a copy of the official receipt from the CNCM depository were submitted with the Response and Amendment. No such documents are found in the file.

6. The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an enabling disclosure commensurate with the scope of the claims. The specification does not adequately teach how to make and use the claimed antibodies as broadly claimed. Those of skill in the art would not know how to effectively make and use the claimed methods with a reasonable expectation of success based on the teachings of the specification and the evidence of record.

a. In part ii, claim 19 is broadly drawn to "a monoclonal antibody which binds to an antigen which the antibody under (i) binds." Thus, the claim is drawn to any antibody that binds to the protein recognized by the monoclonal antibody of I-1397, not antibodies that recognize the same antigenic epitope as I-1397. The specification discloses only that the antibody produced by I-

1397 binds "to a proteinaceous substance having an apparent molecular weight of 48-50K Daltons, as determined by SDS-PAGE" (see p. 7, lines 23-24). With only this information, it would require undue experimentation for one of skill in the art to identify the antibodies claimed.

b. Claims 24-25 are drawn to the treatment of tumors and cancer, and can be broadly interpreted to read on the treatment of any human tumor or cancer with the monoclonal antibodies of the invention. Claims 26-27 are drawn to a pharmaceutical composition, and are also broadly interpreted to read on the treatment of human tumors with monoclonal antibodies. Thus, the present invention pertains to the experimental and unpredictable area of the in vivo treatment of human tumors by the administration of immunoglobulins. As set forth in paragraph 8e of the previous office action, the difficulties associated with the development of effective antibody-based therapies for human cancers are well established in the art. To further illustrate the state of the art, Hird and Epenetos (Immunotherapy with Monoclonal Antibodies, 1990), which states that "data obtained from mouse studies are useful, but cannot be directly translated to apply to the human situation" (p.185) is also cited.

The applicant presents arguments as to the utility of the claimed therapeutic methods. This is not the rejection under consideration. The issue is that the specification does not enable one of skill in the art to practice the claimed invention commensurate with the scope of the claims, to broadly use the claimed methods for treating human tumors and cancers. The specification exemplifies the anti-tumor effect of the claimed monoclonal antibodies in the model systems of lung metastases of MCA fibrosarcoma, B16 melanoma and 3LL tumor cells (both cell lines of mouse origin) in the C57BL and BALB/c mice (see p. 27). From this information, one of skill in the art could not expect to practice the invention as broadly claimed with a reasonable expectation of success.

The applicant alludes to the availability of experimental results shoeing the anti-tumor activity of the monoclonal antibody of he invention in mice bearing human tumors. For such data to be considered by the examiner, it must be presented in declaration format.

7. Claims 19-27 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

8. Claims 20 and 24-27 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. The recitation "A monoclonal antibody ... according to claim 19" lacks clear antecedent basis in claim 19, as there are three different recitations of monoclonal antibody in claim 19.

b. The metes and bounds of "fragment" in claim 20 are unclear. It is unclear what type of fragments are encompassed by the claim. The applicant is advised to amend the claim to recite "antigen binding fragment."

c. The recitation "an effective amount" in claims 24 and 26 is vague and indefinite, as it is unclear what effect is to be achieved by the claimed method and composition.

d. Claim 24 is vague and indefinite in the recitation "so as to affect the immune system." As the specific effect to be

accomplished by the claimed method is unclear, the metes and bounds of the claim are unclear.

9. Claims 19, 21-22, 24 and 26 are rejected under 35 U.S.C. § 102(b) as anticipated by Ledbetter (U.S. Patent No. 5,182,368, filed May 24, 1991). In part ii, the antibody of claim 19 is broadly drawn to "a monoclonal antibody which binds to an antigen which the antibody under (i) binds." Thus, the claim is drawn to any antibody that binds to the protein recognized by the monoclonal antibody of I-1397, not just antibodies that recognize the same antigenic epitope as I-1397. The specification discloses that the antibody produced by I-1397 binds "to a proteinaceous substance having an apparent molecular weight of 48-50K Daltons, as determined by molecular weight" (see p. 7, lines 23-24). Ledbetter discloses a monoclonal antibody that recognizes a polypeptide of approximately 50 Kd (see p.18, lines 45-46), the hybridoma cell line that produces said monoclonal and the use of this antibody to effect the immune system (column 20, lines 1-10). While the antibody of Ledbetter binds to an epitope present only on B cells, there is no evidence of record

that the antibody of Ledbetter and I-1397 recognize distinct protein antigens.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nancy A. Johnson, Ph.D. whose telephone number is (703) 305-5860. The examiner can normally be reached on Monday-Friday from 8:30-5:00. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lila Feisee, can be reached on (703) 308-2731. The fax number for the group is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

LILA FEISEE
SUPERVISORY PATENT EXAMINER
GROUP 1800

Nancy A. Johnson, Ph.D.

November 19, 1996